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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/591,914	09/08/2006	Matthew M. Morrissette	21548YP	1688

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EXAMINER	
SZNAIDMAN, MARCOS L	
ART UNIT	PAPER NUMBER
1612	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/591,914	MORRISSETTE ET AL.	
	Examiner	Art Unit	
	MARCOS SZNAIDMAN	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14 and 19* is/are pending in the application.

4a) Of the above claim(s) *13 and 14* is/are withdrawn from consideration.

5)☒ Claim(s) *11* is/are allowed.

6)☒ Claim(s) *1-9,12 and 14* is/are rejected.

7)☒ Claim(s) *10* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4 pages / 09/08/08 and 02/11/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to applicant's reply filed on June 18, 2008.

Election/Restrictions

Applicant's election with traverse of Group I (Claims 1-12 and 19) and compound of Example 18 as the elected species in the reply filed on June 18, 2008 is acknowledged. The traversal is on the ground(s) that there is unity of invention among the different groups. This is not found persuasive because of "Markush practice" (see MPEP 1850, section III-B).

The requirement is still deemed proper and is therefore made FINAL.

Since the elected species was free of prior art, the search was expanded to the remaining species which are also free of prior art.

Status of Claims

Claims 1-14 and 19 are currently pending and are the subject of this office action.

Claim 13-14 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on June 28, 2008.

Claims 1-12 and 19 are presently under examination.

Priority

The present application is a 371 of PCT/US2005/007106 filed on 03/04/2005, and claims priority to provisional application No. 60/551,440 filed on 03/09/04.

Allowable Subject Matter

Claim 11 is allowed.

Claim Objections

Claim 10 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9, 12 and 19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims 1-9, 12 and 19 recite a compound represented by Formula I (see claim 1) or a pharmaceutical composition comprising a compound of Formula I.

M.P.E.P. #2163 states: "An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention….one must define a compound by 'whatever characteristics sufficiently distinguish it'. A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process".

A description of a chemical genus will usually comprise a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the members of the genus, which features constitute substantial portion of the genus. See *Univ. of California vs. Eli Lilly*, 43 USPQ 2d 1398, 1406 (Fed. Cir. 1997). This is analogous to enablement of a genus under section 112 first, by showing enablement of a representative number of species within the genus. A chemical genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. If the genus has a substantial variance, the disclosure must describe a sufficient number of species to reflect the variation within that genus.

Applicant has failed to show that he was in possession of all the compounds encompassed by Formula I which encompasses millions of compounds (see discussion below). Applicant discloses the structures of 18 compounds (see examples 1-18 on the

specification) all of which show a very narrow set of substituents for R1 through R9. For example, in all the examples R2 = R3 = R4 =R5 = Hydrogen; Z is always Nitrogen; in almost every case R7 and R8 are always Hydrogen, lower alkyl, amide or ester; R1 is always benzyl and R6 is either Hydrogen or Phenyl. This small set of compounds can not be viewed as being reasonably representative of the genus in its claimed scope because no readily apparent combination of identifying characteristics is provided, other than the disclosure of those specific species as examples of the claimed genus.

Given the broad scope of the claimed subject matter, Applicant has not provided sufficient written description that would allow the skilled in the art to recognize all the compounds of formula I claimed.

Claims 1-9, 12 and 19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the compounds listed in claims 10 and 11, does not reasonably provide enablement for the remaining compounds claimed in formula I. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. This is a scope of enablement rejection.

To be enabling, the specification of the patent application must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557, 1561 (Fd. Cir. 1993). Explaining what is meant by "undue experimentation," the Federal Circuit has stated that:

The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. PPG v. Guardian, 75 F.3d 1558, 1564 (Fed. Cir. 1996). As pointed out by the court in *In re Angstadt*, 537 F.2d 498 at 504 (CCPA 1976), the key word is "undue", not "experimentation".

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 wherein, citing *Ex parte Forman*, 230 USPQ 546 (Bd. Apls. 1986) at 547 the court recited eight factors:

1- the quantity of experimentation necessary,

2- the amount of direction or guidance provided,

3- the presence or absence of working examples,

4- the nature of the invention,

5- the state of the prior art,

6- the relative skill of those in the art,

7- the predictability of the art, and

8- the breadth of the claims

These factors are always applied against the background understanding that scope of enablement varies inversely with the degree of unpredictability involved. *In re Fisher*, 57 CCPA 1099, 1108, 427 F.2d 833, 839, 166 USPQ 18, 24 (1970). Keeping that in mind, the *Wands* factors are relevant to the instant fact situation for the following reasons:

1. <u>The nature of the invention</u>

Claims 1-9, 12 and 19 recite a compound represented by formula I (see claim 1) or a pharmaceutical composition comprising a compound of formula I.

2. The relative skill of those in the art

The relative skill of those in the art is high, generally that of an M.D. or Ph.D. The artisan using Applicant's invention would generally be a physician with a M.D. degree and several years of experience.

3. The state and predictability of the art

Since the compounds of claim 1 are novel there is no synthetic procedure for these particular compounds in the prior art.

It is well know in the prior art that organic synthesis is still an experimental science. Even though the knowledge of organic synthesis and the arsenal of chemical reactions have exploded in the last decades, there is still a high degree of unpredictability in organic synthesis. See for example Dorwald F. A. (Side reactions in organic synthesis, 2005, Wiley, VCH, Weinheim, pg. IX of Preface) where it says: " Most non-chemists would probably be horrified if they were to learn how many attempted synthesis fail, and how inefficient research chemists are. The ratio of successful to unsuccessful chemical experiments in a normal research laboratory is far below unity, and synthetic research chemists, in the same way as most scientists, spend most of their time working on what went wrong, and why. He later states: "The final synthesis usually looks like quite different from that originally planned, because of unexpected

difficulties encountered in the initially chosen synthetic sequence. Only the seasoned practitioner who has experienced for himself the many failures and frustrations which the development (sometimes even repetition) of a synthesis usually implies will be able to appraise such work". And finally: "Chemists tend not to publish negative results, because these are, as opposed to positive results, never definitive (and far too copious)."

4. The breadth of the claims

Claims 1-9, 12 and 14 are very broad in terms of the number of compounds claimed.

5. The amount of direction or guidance provided and the presence or absence of working examples

MPEP 2164.03 cites: "the amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more

detail as to how to make and use the invention in order to be enabling. See, e.g., Chiron Corp. v. Genentech Inc., 363 F.3d 1247, 1254, 70 USPQ2d 1321, 1326 (Fed. Cir. 2004) ("Nascent technology, however, must be enabled with a specific and useful teaching.' The law requires an enabling disclosure for nascent technology because a person of ordinary skill in the art has little or no knowledge independent from the patentee's instruction. Thus, the public's end of the bargain struck by the patent system is a full enabling disclosure of the claimed technology."

Applicant provides general synthetic schemes (see schemes 1 through 9) for some of these compounds. However, even though applicant claims an extensive and diverse set of substituents for R1 through R9 (see claim 1); the actual compounds disclosed (18 total, see examples 1 through 18) show a very narrow and defined set of substituents: for example in all the examples R2 = R3 = R4 =R5 = Hydrogen; Z is always Nitrogen; in almost every case R7 and R8 are always Hydrogen, lower alkyl, amide or ester; R1 is always benzyl and R6 is either Hydrogen or Phenyl. There are no examples wherein all R groups are for example aromatic or substituted alkyl or any other functional group.

6. The quantity of experimentation necessary

As discussed above (see: 3. the state and predictability of the art), small changes in the structure of one of the reagents could cause a completely different synthetic outcome (i.e. different products, lower yields or no reaction at all). Based on this, and since applicant claims such a diverse set of substituents (from small alkyl groups all the

way up to heterocycles (see: 5. The amount of direction or guidance and the presence or absence of working examples above) it is expected that some, if not most of the R substituents recited in claim 1 (except for those specifically listed in claims 10 and 11) will not provide the desired synthetic outcome outlined by applicant in schemes 1 through 9. For example applicant introduces R2 as in synthetic scheme 4, or R4 as in synthetic scheme 5, but none of these synthetic procedures explain how to make a compound when both R2 and R4 are different then Hydrogen, or how to make a compound of formula I when both R2 and R3 are different than Hydrogen, etc.

So, determining how to make a particular compound with an R1, R2, R3, etc. group not included in claims 10 and 11 would require testing of new synthetic pathways for the different compounds. This is undue experimentation given the limited guidance and direction provided by Applicants.

Accordingly, the inventions of claims 1-9, 12 and 19 do not comply with the enablement requirement of 35 U.S.C 112, first paragraph, since to practice the claimed invention a person of ordinary skill in the art would have to engage in undue experimentation with no assurance of success.

Conclusion

Claims 1-9, 12 and 19 are rejected.

Claim 10 is objected.

Claim 11 is allowed.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARCOS SZNAIDMAN whose telephone number is (571)270-3498. The examiner can normally be reached on Monday through Thursday 8 AM to 6 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick F. Krass can be reached on 571 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/MARCOS SZNAIDMAN/
Examiner, Art Unit 1612
October 14, 2008

/Brandon J Fetterolf/
Primary Examiner, Art Unit 1642